REMARKS

I. Status of the Claims

Claims 1-15 were pending in this application. The Office withdrew claims 8, 9, and 12-15 as being directed to a non-elected invention. With entry of this Amendment, Applicants have cancelled claims 5, 8, 9, and 12-15, without prejudice or disclaimer, and amended claims 1, 4, 10, and 11. Applicants thank the Office for its consideration in withdrawing a portion of the previous restriction requirement (rejoining group 1 (claims 1-7 and 10) and group II (claims 2-7 and 11)). Thus, claims 1-7, 10, and 11 are pending and stand rejected.

II. Objections to the Specification and Sequence Listing

The Office objects to the Specification under 35 U.S.C. § 132 because the Amendment filed on January 13, 2003, allegedly introduces new matter. Office action, pages 3-4. Specifically, the Office contends that the substitute Sequence Listing filed with that previous Amendment introduces new matter because it truncates a single uracil residue from the 3' end of SEQ ID No. 1 and SEQ ID No. 2. According to the Office, these are not the same sequences as disclosed in the original Specification. *Id.*, pages 3 and 4. The Office similarly rejects the substitute Sequence Listing as not complying with 37 C.F.R. 1.821 through 1.825, because the sequences in the Sequence Listing do not match the corresponding sequences in the Specification. *Id.*, page 4.

In response, Applicants note that SEQ ID No. 1 and SEQ ID No. 2 are based on originally filed Figures 1B and 1C, respectively. This is clear from the <220> field identifier in the original and substitute Sequence Listings. The <220> field indicates that SEQ ID No. 1 represents the sequence of Rz2, and SEQ ID No. 2 represents the

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sequence of Rz3. Figure 1B as originally filed provides the correct sequence of Rz2 (SEQ ID No. 1). Figure 1C as originally filed provides the correct sequence of Rz3 (SEQ ID No. 2). The sequences represented in Figures 1B and 1C both have 4 uracils at their 3' ends, rather than 5 uracils. These figures provide the correct sequences. Although the original Sequence Listing recited 5 uracils at the end of SEQ ID Nos. 1 and 2, this was corrected in the substitute sequence listing to conform with the sequences provided in Figures 1B and 1C. Since this amendment is clearly supported by the originally filed figures, no new matter has been introduced by this sequence listing.

In presenting the substitute sequence listing, Applicants failed to enter a corresponding amendment that also corrected SEQ ID No. 1 and 2 in the actual text of the Specification. With entry of this Amendment, the recitations of these sequences in the text of the Specification has been corrected to recite only four uracils at the end of SEQ ID Nos. 1 and 2. As these correct sequences were disclosed in originally-filed Figures 1B and 1C, no new matter has been introduced. Accordingly, Applicants respectfully request that the Office withdraw the new matter objection to the Specification and the objection to the Substitute Sequence Listing.

III. Submission of Corrected Drawing

The Office notes that sequences in Figure 2 have not been identified by SEQ ID Nos. In response, Applicants have corrected Figure 2 to recite the proper SEQ ID Nos. for each sequence (SEQ ID Nos. 24 and 25). Applicants have enclosed a clean copy of the corrected figure, and also a marked-up copy indicating the proposed changes in red ink. No new matter has been introduced by this amendment. Subject to the approval of

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the Examiner, please replace Figure 2 with the corrected Figure 2 submitted herewith. Applicants respectfully request that the Office withdraw the objection to Figure 2.

IV. Written Description Rejection

The Office has rejected claims 1-7, 10, and 11, under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention. Office action, page 6. The Office indicates that this is a new matter rejection, because SEQ ID Nos. 1 and 2 in the substitute Sequence Listing do not match the corresponding sequences in the Specification. *Id.* As noted above, the sequences in the substitute Sequence Listing are based on SEQ ID Nos. 1 and 2, as set forth in original Figures 1B and 1C, respectively. Thus, the amended sequences in the substitute Sequence Listing are supported by the original disclosure and no new matter has been introduced. To maintain consistency in the Specification, Applicants have also amended the text where SEQ ID Nos. 1 and 2 are recited in the Specification so that the sequences conform with the correct sequences in Figures 1B and 1C. Accordingly, Applicants respectfully request that the Office withdraw this rejection.

V. Indefiniteness Rejection

The Office has rejected claims 1-7, 10, and 11, under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Office action, page 5. The Office rejects claims 1-7 for reciting SEQ ID Nos. 1 and 2, wherein these sequences, as provided in the substitute Sequence Listing, differ from the corresponding sequences recited in the Specification. *Id.* As noted above, the sequences in the substitute Sequence Listing

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are based on SEQ ID Nos. 1 and 2, as set forth in original Figures 1B and 1C, respectively. To better clarify the claimed invention, Applicants have amended the claims and the Specification such that SEQ ID Nos. 1 and 2 are identical to those recited in Figures 1B and 1C, and the substitute Sequence Listing. Accordingly, Applicants respectfully request that the Office withdraw the rejection.

The Office also rejected claims 10 and 11 because they are dependent upon a non-elected base claim. Office action, pages 4-5. Additionally, the Office contends that claim 10 is indefinite because it recites a variant consisting of 80 nucleotides, but depends from claim 8, which recites a structure containing 94 nucleotides. *Id.*, page 5. Similarly, the Office rejects claim 11 because it contains a variant consisting of 86 nucleotides, but depends from claim 8, which recites a structure containing 94 nucleotides. *Id.* As claim 8 is no longer pending, Applicants have amended claims 10 and 11 into independent form. Accordingly, these rejections are no longer applicable and Applicants respectfully request that the Office withdraw them.

VI. Enablement Rejection

The Office has rejected claims 3-7, under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Office action, pages 6-10. According to the Office, the specification fails to provide sufficient guidance to make and use the claimed ribozymes *in vivo*. Office action, page 7.

Applicants respectfully disagree and traverse the rejection. To further prosecution of this application, however, Applicants have amended claim 4 and canceled claim 5, without prejudice or disclaimer. Presently amended claim 4 is directed to a composition rather than a pharmaceutical composition. Because amended

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claim 4 does not recite a "pharmaceutical composition," the claimed composition is not limited to *in vivo* uses. Given that the Office admits the specification enables one of skill in the art to make and use the invention *in vitro* (Office action, pages 6 and 7), this amendment obviates the enablement rejection of claim 4. Applicants reserve the right to pursue the canceled subject matter in one or more future applications.

In traversing the rejection, Applicants note that the relevant inquiry for enablement is whether one of skill in the art could make or use the invention from the disclosure in the specification, coupled with information known in the art, without undue experimentation. *See* M.P.E.P. § 2164.01. The test for undue experimentation, however, does not depend on the amount of experimentation, since a considerable amount is permissible, as long as it is routine. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Moreover, a patent need not teach, and preferably omits what is well known in the art. *See* M.P.E.P. § 2164.01, and cases cited therein.

Applicants contend that one of skill in the art, reading the teaching of the specification, would know how to make and use the presently claimed invention without undue experimentation. Applicants respectfully remind the Office that the specification needs only to enable a single method making and using the claimed invention. As long as the specification discloses at least one method for making and using the claimed invention, the enablement requirement of 35 U.S.C. § 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970); M.P.E.P. § 2164.01(b). It is not necessary to disclose other methods by which the claimed invention may be made. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533 (Fed. Cir. 1987). The Office has already

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acknowledged that Applicants have met this threshold for objective enablement, stating that the present Specification is "enabling for a method of making a ribozymes by transcribing a vector in vitro (cell culture, a method cleaving mRNA in vitro (cell culture), and a composition comprising a ribozymes or vector and a pharmaceutically acceptable carrier." Office action, pages 6-7. Thus, the specification enables a method of making and using the presently claimed invention, at the very least, in cell culture. Given this admission by the Office, Applicants contend that the enablement requirement of 35 U.S.C. § 112, first paragraph, is satisfied

Despite the clear enablement for *in vitro* uses of the claimed invention, the Office contends that the claims still lack enablement because they encompass non-enabled *in vivo* uses, that is, gene therapy. Office action, page 7. In support of this contention, the Office cites a number of scientific publications that report the unpredictability of using ribozymes in whole organisms and various problems with delivering the appropriate genetic material to the organisms via gene therapy. Applicants point out, however, that the claims are in no way limited to gene therapy or *in vivo* use. Rather, the claims embrace many other applications that do not involve gene therapy.

For example, as noted by the Office, "the Specification provides examples wherein antisense is delivered to cells *in vitro* and HIV RNA is cleaved and replication is inhibited . . .." Office action, page 9. This highlights an important use of the present invention, namely, as a system for regulating target gene transcription in a cell. *See, e.g.*, Specification, pages 13, 33, 37-40. As the Specification also states, the tRNA ribozymes of the present invention "have consistently high activities" in cultured cells, and are therefore "very useful as tools in molecular biology." Specification, page 40,

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lines 16-22. When multiple uses are described, it is only necessary for Applicants to enable one of the uses. "[I]f any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." M.P.E.P. 2164.01(c). It is not necessary for Applicants to enable additional methods of making and using the claimed ribozymes (*e.g.*, *in vivo*) in order to satisfy the requirements of § 112, first paragraph.

In summary, Applicants have satisfied the requirements of § 112, first paragraph by providing an enabling disclosure of various methods for making and using the claimed invention, at the very least, in cell culture. Moreover, the Office has acknowledged that these methods are enabling. Contrary to the Office's position, it is not necessary for Applicants to provide additional methods of making and using the invention (*e.g.*, *in vivo*) in order to enable the present claims. Only a single method of making and using need be disclosed. Applicants have clearly met this threshold requirement. Accordingly, Applicants respectfully request that the Office withdraw the rejection of claims 3-7, under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicants contend that the present case is in condition for allowance and respectfully request early notification of such. If any fees are necessary for entering this response, please charge our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: August 7, 2003

By: _____
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